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## Search History

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USPT	16 not 17	136	<a href="#">L8</a>
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USPT	antisense or anti-sense or anti sense	8819	<a href="#">L5</a>
USPT	11 or 12	3174	<a href="#">L4</a>
USPT	nitricoxide synthase	0	<a href="#">L3</a>
USPT	inos	2792	<a href="#">L2</a>
USPT	nitric oxide synthase	474	<a href="#">L1</a>

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L7 Entry 2 of 5

File: USPT

Nov 3, 1998

DOCUMENT-IDENTIFIER: US 5830848 A

TITLE: Method and agents for inducement of endogenous nitric oxide synthase for control and management of labor during pregnancy

DEPR:

FIG. 14 is a photograph of in situ hybridization with a rat iNOS cDNA antisense probe for localization of iNOS expression in the pregnant rat uterus at day 16 (FIG. 14A); in the decidua basalis (FIG. 14B), in myocytes (FIGS. 14C and 14D).

DEPR:

The augmentation of uterine NO production is achieved by administration of agents enhancing the capacity of the uterus to make endogenous uterine NO. Such endogenous uterine NO production constituting endogenous tocolytic effect is achieved through administration of agents having a uterine-selective effect on iNOS in the myometrium. Such agents include systemically or by any other conventional route administered cytokines, growth factors, or sense or antisense oligonucleotides. Exemplary cytokines are Inf .gamma., IL-1.beta., IL-6, IL-8, TNF-.alpha., CSF-1, GM-CSF and TGF-.beta.. Exemplary growth factors are epidermal growth factor (EGF), fibroblast growth factors (FGFs), eicosanoids, alone or in combination with hormones such as progesterone or estradiol 17.beta., of which the levels are very high in pregnancy acting as an adjuvant. Exemplary sense or antisense oligonucleotides are antisense oligonucleotides directed against iNOS gene promoter repressor elements, or sense oligonucleotides directed towards iNOS gene promoter or promoters of genes for iNOS gene transcriptional regulators, which selectively increase uterine NO production. These agents are also delivered to the uterus in a targeted manner, for example, by complexing these agents with other biomolecules, such as hormones, antibodies, or nutrients, which are selectively taken up by or concentrated within the uterus or myometrium. Specific examples of these targeting techniques are complexing an agent with an oxytocin receptor antagonist, complexing an agent with an antibody directed to a uterine-specific antigen, and using liposomal carriers to deliver agents.

DEPR:

The all above discussed results of in vitro studies support the current invention and confirm results of in vivo studies which show that nitric oxide is directly involved in maintaining uterus relaxation during pregnancy. When the endogenous levels or availability of nitric oxide decrease, the uterus respond with increased contractility resulting in labor. When this occurs prior to normal term of pregnancy, such decreased level of nitric oxide results in preterm labor. By providing exogenous nitric oxide source or donor, the preterm contractions can be inhibited and the preterm labor stopped before resulting in preterm delivery. By providing agents hormones such as cytokines growth factors or sense or antisense oligonucleotides, the level of iNOS expression can be enhanced to prevent development or reverse onset of or stop premature labor.

DEPR:

For endogenous control of preterm labor through induction of increased production of NO by increased expression of iNOS, hormones, cytokines, growth factors, or sense or antisense oligonucleotides are administered in any suitable route described above.

**McGarry, Sean**

To: STIC-ILL  
Subject: reference request  
Importance: High

Please forward the following references to  
Sean McGarry  
AU 1635  
CM1 11D07

L12 ANSWER 68 OF 79 CAPLUS COPYRIGHT 2000 ACS  
AN 1996 324381 CAPLUS  
DN 125:54131  
TI A first stable inducible \*\*\*nitric\*\*\* \*\*\*oxide\*\*\* \*\*\*synthase\*\*\*  
\*\*\*antisense\*\*\* macrophage cell line  
AU Bosse, Geraldine; Fischer, Hans-Georg; Rothe, Helga  
CS Diabetes Research Institute, Heinrich-Heine University, Duesseldorf,  
40225, Germany  
SO Portland Press Proc. (1996), 10(Biology of Nitric Oxide Part 5), 142  
CODEN: POPPEF  
DT Journal  
LA English

L12 ANSWER 67 OF 79 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1996:255108 BIOSIS  
DN PREV199698811237  
TI Inducible \*\*\*nitric\*\*\* \*\*\*oxide\*\*\* \*\*\*synthase\*\*\* : The use of  
\*\*\*antisense\*\*\* oligodeoxynucleotides to study its regulation and role  
in neoplastic transformation.  
AU Lesoon-Wood, L. A.; Lau, A. F.; Cooney, R. V.  
CS Mol. Carcinogenesis, Cancer Res. Cent., Honolulu, HI 96813 USA  
SO Proceedings of the American Association for Cancer Research Annual  
Meeting, (1996) Vol. 37, No. 0, pp. 145.  
Meeting Info.: 87th Annual Meeting of the American Association for Cancer  
Research Washington, D.C., USA April 20-24, 1996  
ISSN: 0197-016X.  
DT Conference  
LA English

L12 ANSWER 61 OF 79 MEDLINE DUPLICATE 28  
AN 97144252 MEDLINE  
DN 97144252  
TI Evidence for a physiological role for nitric oxide in the regulation of  
the LH surge: effect of central administration of \*\*\*antisense\*\*\*  
oligonucleotides to \*\*\*nitric\*\*\* \*\*\*oxide\*\*\* \*\*\*synthase\*\*\* .  
AU Aguan K; Mahesh V B; Ping L; Bhat G; Brann D W  
CS Department of Physiology and Endocrinology, Medical College of Georgia,  
Augusta 30912-2000, USA  
J. Neuroendocrinol. 1997;17(1):1-6.  
Journal Code: NYN ISSN: 0028-3831  
Ch Switzerland

DI Journal: Article: (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199706  
EW 19970601

L12 ANSWER 60 OF 79 MEDLINE DUPLICATE 27  
AN 96295522 MEDLINE  
DN 96295522  
TI \*\*\*Antisense\*\*\* evidence for two functionally active forms of  
\*\*\*nitric\*\*\* \*\*\*oxide\*\*\* \*\*\*synthase\*\*\* in brain microvascular  
endothelium.  
AU Rosenblum W I; Murata S  
CS Department of Pathology (Neuropathology), Medical College of  
Virginia/Virginia Commonwealth University, Richmond 23298-0017, USA.  
NC HL35935 (NHLBI)  
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996 Jul 16) 224 (2)  
535-43.  
Journal code: 9Y8. ISSN: 0006-291X.  
CY United States  
DT Journal: Article: (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; Cancer Journals  
EM 199611

L12 ANSWER 43 OF 79 MEDLINE DUPLICATE 19  
AN 97368347 MEDLINE  
DN 97368347  
TI Functionally differentiating two neuronal \*\*\*nitric\*\*\* \*\*\*oxide\*\*\*  
\*\*\*synthase\*\*\* isoforms through \*\*\*antisense\*\*\* mapping: evidence  
for opposing NO actions on morphine analgesia and tolerance.  
AU Kolesnikov Y A; Pan Y X; Babey A M; Jain S; Wilson R; Pasternak G W  
CS The Cotzias Laboratory of Neuro-Oncology and Departments of Neurology and  
Anesthesiology, Memorial Sloan-Kettering Cancer Center, New York, NY  
10021, USA.  
NC DA07242 (NIDA)  
DA00220 (NIDA)  
DA00296 (NIDA)  
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF  
AMERICA, (1997 Jul 22) 94 (15) 8220-5.  
Journal code: PV3. ISSN: 0027-8424.

L12 ANSWER 42 OF 79 CAPLUS COPYRIGHT 2000 ACS  
AN 1997:168560 CAPLUS  
DN 126:152830  
TI Vascular endothelial growth factor receptor gene regulator screening,  
antisense and gene therapy, and cancer inhibitors, antiarteriosclerotics,  
and angiogenesis regulation  
IN Patterson-Winston, Campbell; Lee, Mu-En; Haber, Edgar  
PA President and Fellows of Harvard College, USA  
SO PCT Int. Appl., 69 pp.  
CODEN: PIXXD2

PATENT NO. AND DATE OF FILING AND NO. DATE

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PI WO 9700957 A1 19970109 WO 1996-US10725 19960621  
W: AU, CA, IL, JP, MX, NO  
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
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